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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,523	11/07/2001	Jiri Snaidr	235.017US1	9919

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EXAMINER	
SAKELARIS, SALLY A	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/008,523	SNAIDR, JIRI	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *72003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Applicant

This action is written in response to applicant's correspondence submitted 10/6/2003. Claim 1 has been amended, and claim 28 has been added and claims 25-27 are withdrawn following their non-election. Claims 1-24 and 28 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

THE FOLLOWING ARE NEW REJECTIONS NECESSITATED BY APPLICANT'S AMENDMENTS TO THE CLAIMS

Priority

Acknowledgement of claim to foreign priority of German Applications, 19921281.3, filed 5/7/1999 and 19936875.9 filed 8/05/1999 under 35 U.S.C. 119(a)-(d) has been made, however applicant should note that the certified translations of these foreign priority documents have not yet been received and as a result the claim to foreign priority under the same has not yet been granted.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 6, 9-13, 15-17, 19-23, and New claim 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Guillot et al.(WO 99/18234, 15 April 1999).

The reference teaches a method of detecting microorganisms in a sample by means of detectable nucleic acid probe molecules comprising the following steps:

a) fixing the microorganisms contained in the sample;(Pg. 3, Pg. 6 lines 10-27)

b) incubating the fixed microorganisms with the detectable nucleic acid probe molecules(Pg 7, lines 3-19) that are complementary to rRNA;(Pg 2-3 esp. 3 lines 18-21)

c) removing nonhybridized nucleic acid probe molecules;(Pgs 7-8 lines 20-3)

d) separating hybridized nucleic acid probe molecules at 100°C without using formamide, under conditions that provide more detectable separated nucleic acid probe molecules than corresponding hybridized nucleic acid molecules separated using formamide through the use of "probe target denaturing agent such as one that will separate duplex DNA/DNA or DNA/RNA"(Pg. 8 lines 5-9 and claim 14)

e) detecting and quantifying the separated nucleic acid probe molecules.(Pg. 8 lines 19-28)

The reference further teaches the above method wherein the detectable nucleic acid probe molecules comprise nucleic acid probe molecules covalently bonded to a detectable marker, such as a radioactive marker(Pg. 8 lines 19-28). In addition the reference teaches the above method for detecting microorganisms wherein the microorganism is a single-cell microorganism and a bacterium(Pgs 4-5 lines 19-14). Guillot et al. teach the above method, wherein the sample is an environmental sample taken from the water, soil and air(Pg. 9 line 6-11); wherein the sample is a food sample taken from drinking water(Pg. 9 line 6); wherein the sample is taken from

secretions(ex. urine, vaginal Pg. 9 line 11); wherein the sample is taken from wastewater(""line 7), activated sludge(Pg. 10 line 20), wherein the sample is from industrial effluent("biofilm" as defined on page 15 of specification), organic effluent(Pgs.1, 9, or claim 18).

Response to Arguments:

While Applicant submits that WO 99/18234 is not available as a reference under 35 U.S.C. §102(b), the rejection is maintained as applicant's claim to foreign priority has not yet been granted. Applicant further traverses this rejection on the grounds that the Guillot et al. reference teaches that "the preferred denaturing agent is formamide" and that "while Guillot et al. generally disclose the use of denaturing agents to extract hybridized probes, there is nothing in the Guillet et al. reference that teaches or suggests the separation of hybridized nucleic acid probe molecules without using formamide under conditions that provide more detectable separated nucleic acid probe molecules than corresponding hybridized nucleic acid molecules separated using formamide"(Applicant's Response Pg. 8). This argument is not convincing as on page 8 lines 5-9 of the reference, WO 99/18234 asserts that the extraction of the probes can occur "in the presence of a probe-target denaturing agent such as one that will separate duplex DNA/DNA or DNA /RNA". The examiner maintains that in the absence of any evidence to the contrary, it is a property of any method in which the formamide is omitted that such a method allows for the detection of more detectable separated nucleic acid probe molecules than corresponding hybridized nucleic acid molecules. Furthermore, the claims are not limited to special conditions lacking formamide, ie., conditions without formamide but with the specific inclusion of other reagents/conditions. The claim requires only the absence of formamide. The specification has not taught any particular conditions that must be used in combination with the

absence of formamide to achieve the result of providing more detectable separated probe molecules than corresponding hybridized nucleic acid molecules.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-13, 15-17, and 19-23 and New claim 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guillot et al.(WO 99/18234, 15 April 1999) in view of Roe et al.(DNA isolation and sequencing, 1996), and in further view of Kemp et al.(US Patent 6,090,627).

Guillot et al. teach a method of detecting microorganisms in a sample by means of detectable nucleic acid probe molecules comprising the following steps:

a) fixing the microorganisms contained in the sample;(Pg. 3, Pg. 6 lines 10-27)

b) incubating the fixed microorganisms with the detectable nucleic acid probe molecules(Pg 7, lines 3-19) that are complementary to rRNA;(Pg 2-3 esp. 3 lines 18-21)

c) removing non-hybridized nucleic acid probe molecules;(Pgs 7-8 lines 20-3)

d) separating hybridized nucleic acid probe molecules at 100°C without using formamide, under conditions that provide more detectable separated nucleic acid probe molecules than corresponding hybridized nucleic acid molecules separated using formamide through the use of "probe target denaturing agent such as one that will separate duplex DNA/DNA or DNA/RNA"(Pg. 8 lines 5-9 and claim 14)

through the use of "probe target denaturing agent such as one that will separate duplex DNA/DNA or DNA/RNA"(Pg. 8 lines 5-9 and claim 14)

e) detecting and quantifying the separated nucleic acid probe molecules.(Pg. 8 lines 19-28)

The reference further teaches the above method wherein the detectable nucleic acid probe molecules comprise nucleic acid probe molecules covalently bonded to a detectable marker, such as a radioactive marker(Pg. 8 lines 19-28). In addition the reference teaches the above method for detecting microorganisms wherein the microorganism is a single-cell microorganism and a bacterium(Pgs 4-5 lines 19-14). Guillot et al. teach the above method, wherein the sample is an environmental sample taken from the water, soil and air(Pg. 9 line 6-11); wherein the sample is a food sample taken from drinking water(Pg. 9 line 6); wherein the sample is taken from secretions(ex. urine, vaginal Pg. 9 line 11); wherein the sample is taken from wastewater(""line 7), activated sludge(Pg. 10 line 20), wherein the sample is from industrial effluent("biofilm" as defined on page 15 of specification), organic effluent(Pgs.1, 9, or claim 18). Guillot et al. teach the use of any denaturing agent in the method's step d).

Guillot et al. do not exemplify said method of detecting wherein the denaturing agent present in step d), is in a separation solution of water consisting of 0.001- 1.0 M Tris/HCl, pH 9.0 +/- 2.0 nor do they teach the solution to be incubated at a temperature lower than 100°C or approximately at 80°C.

However, Roe et al. teach this embodiment of water as a denaturing agent in their 10X denaturing buffer consisting of 200mM Tris-HCl, pH 9.5, 1mM EDTA, and 10mM spermidine

all in double distilled water. Furthermore, Kemp et al. also teach a denaturing buffer with 20 mM Tris/HCl and a pH of 9.5 being incubated at 70°C.

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to have practiced the claimed method taught by Guillot et al. of using a "denaturing agent" in step d) wherein the denaturing agent, was contained in the "denaturing buffer" of Roe et al. in order to provide a solution with double distilled water as the denaturing agent in conjunction with the use of Tris/HCl concentrations and the proper pH as exemplified by Kemp et al. with which to denature the hybridized probes for subsequent, accurate quantification as the Tris/Hcl solution is equally as effective means to release the bound probes. With respect to claims 5 and 8 especially, it then would have been further obvious to augment the Tris/HCl concentration and temperature of the separation solution within the limits taught by Roe and Kemp et al. as optimization of conditions for performing a method step are well within the skill of the art. As discussed in MPEP2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955).

Response to Arguments:

Applicant's traversal concerning Guillot et al. reference is responded to above following the maintained, 102(b) rejection. Applicant's arguments concerning the Roe et al. reference include the assertion that the reference "does not disclose or suggest whether the solutions disclosed therein are suitable for use in a method of detecting nucleic acids fixed microorganisms". Concerning the Kemp et al. reference, applicant asserts that the reference "does not teach or suggest a method of detecting the nucleic acid of fixed microorganisms in a

sample"(Pg. 10 response). With respect to the above rejection over Guillot et al., Roe et al., and Kemp et al., applicant asserts that Roe et al. and Kemp et al. do not remedy the deficiencies of Guillot et al. and that neither Roe et al. or Kemp et al. provides one skilled in the art with a reasonable expectation that the instantly claimed methods of detecting microorganisms in a sample could have been carried out. Lastly, applicant asserts that the examiner omitted a suggestion or motivation to combine these above references and further that there is no motivation to combine the cited documents because they come from non-analogous art. However, the examiner find these arguments to be unconvincing and maintains the rejection and points applicant to the last paragraph in the rejection where the expected benefit and motivation for combining the references can be found. The examiner also maintains that each of these references concern the same subject matter classified in Class 435 subclass 6 and as a result, steps of optimization, as discussed in MPEP2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955).

4. Claims 14, 18, and 24 and 1, 2, 6, 9-13, 15-17, 19-23 and New claim 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guillot et al.(WO 99/18234, 15 April 1999) in view of Sanders et al.(US Patent 5,888,725)

Guillot et al. teach a method of detecting microorganisms in a sample by means of detectable nucleic acid probe molecules comprising the following steps:

a) fixing the microorganisms contained in the sample;(Pg. 3, Pg. 6 lines 10-27)

b) incubating the fixed microorganisms with the detectable nucleic acid probe molecules(Pg 7, lines 3-19) that are complementary to rRNA;(Pg 2-3 esp. 3 lines 18-21)

c) removing nonhybridized nucleic acid probe molecules;(Pgs 7-8 lines 20-3)

d) separating hybridized nucleic acid probe molecules at 100°C without using formamide, under conditions that provide more detectable separated nucleic acid probe molecules than corresponding hybridized nucleic acid molecules separated using formamide through the use of "probe target denaturing agent such as one that will separate duplex DNA/DNA or DNA/RNA"(Pg. 8 lines 5-9 and claim 14)

e) detecting and quantifying the separated nucleic acid probe molecules.(Pg. 8 lines 19-28)

The reference further teaches the above method wherein the detectable nucleic acid probe molecules comprise nucleic acid probe molecules covalently bonded to a detectable marker, such as a radioactive marker(Pg. 8 lines 19-28). In addition the reference teaches the above method for detecting microorganisms wherein the microorganism is a single-cell microorganism and a bacterium(Pgs 4-5 lines 19-14). Guillot et al. teach the above method, wherein the sample is an environmental sample taken from the water, soil and air(Pg. 9 line 6-11); wherein the sample is a food sample taken from drinking water(Pg. 9 line 6); wherein the sample is taken from secretions(ex. urine, vaginal Pg. 9 line 11); wherein the sample is taken from wastewater(""line 7), activated sludge(Pg. 10 line 20), wherein the sample is from industrial effluent("biofilm" as defined on page 15 of specification), organic effluent(Pgs.1, 9, or claim 18).

Guillot et al. do not exemplify said method of detecting wherein the microorganism to be detected belongs to the genus *Salmonella* nor the method of detecting wherein the sample is a medicinal one or is taken from a pharmaceutical product.

However, Sanders et al teaches a method for detection, identification and/or quantification of target organisms of specific bacterial genus, based upon the occurrence of nucleotides, specifically for the genus *Salmonella.* The method of the present invention has more readily realized potential for the specific and rapid detection of almost any bacteria in any environmental or forensic sample(foodstuffs, drinking water, pharmaceutical products and diseased tissues in humans, animals, and plants etc.). The reference further teaches that the present invention has been shown to be capable of detection of a single *Salmonella* in a 1 ml sample of milk in under 12 hours.(Column 2 lines 11-19).

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to have practiced the claimed method taught by Guillot et al. for the detection of microorganism in light of the method taught by Sanders et al. to specifically detect *Salmonella* in medicinal and pharmaceutical samples, for the expected benefit of a specific and rapid detection system for almost any bacteria in any environment.

Response to Arguments:

Applicant asserts that that Sanders et al. do not remedy the deficiencies of Guillot et al. as neither Guillot et al. or Sanders et al. teach a method in which hybridized nucleic acid probes are separated without using formamide under conditions that provide more detectable separated nucleic acid probe molecules than corresponding hybridized nucleic acid molecules separated using formamide. However, the examiner maintains the rejection on the grounds that the claims

are not limited to special conditions including both the absence of formamide and the inclusion of other reagents. As such the art as cited, obviates the above claims.

5. Claims 1-24 and New claim 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guillot et al.(WO 99/18234, 15 April 1999), in view of Roe et al.(DNA isolation and sequencing, 1996), in further view of Kemp et al.(US Patent 6,090,627), and in even further view of Sanders et al.(US Patent 5,888,725).

Please see above(#3.) for the teachings of Guillot et al.(WO 99/18234, 15 April 1999), in view of Roe et al.(DNA isolation and sequencing, 1996), in further view of Kemp et al.(US Patent 6,090,627).

Guillot et al.(WO 99/18234, 15 April 1999), in view of Roe et al.(DNA isolation and sequencing, 1996), in further view of Kemp et al.(US Patent 6,090,627) do not exemplify this method of detecting wherein the microorganism to be detected belongs to the genus *Salmonella* nor the method of detecting wherein the sample is a medicinal one or is taken from a pharmaceutical product.

However, Sanders et al teaches a method for detection, identification and/or quantification of target organisms of specific bacterial genus, based upon the occurrence of nucleotides, specifically for the genus *Salmonella.* The method of the present invention has more readily realized potential for the specific and rapid detection of almost any bacteria in any environmental or forensic sample(foodstuffs, drinking water, pharmaceutical products and diseased tissues in humans, animals, and plants etc.). The reference further teaches that the present invention has been shown to be capable of detection of a single *Salmonella* in a 1 ml sample of milk in under 12 hours.(Column 2 lines 11-19).

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to have practiced the claimed method taught by Guillot et al.(WO 99/18234, 15 April 1999), in view of Roe et al.(DNA isolation and sequencing, 1996), in further view of Kemp et al.(US Patent 6,090,627) for the detection of microorganism in light of the method taught by Sanders et al. to specifically detect *Salmonella* in medicinal and pharmaceutical samples, for the expected benefit of a specific and rapid detection system for almost any bacteria in any environment.

Response to Arguments:

Applicant asserts that while a motivation existed to combine these above references, "the methods disclosed in Guillot et al., Roe et al., Kemp et al., and Sanders et al. are quite different", and as a result the provided motivation would not be sufficient. Furthermore, the applicant asserts that even if the motivation was present the combination would not result in the instantly claimed method as none of the cited documents discloses or suggests a method which hybridized nucleic acid probes are separated without using formamide under conditions that provide more detectable separated nucleic acid probe molecules than corresponding hybridized nucleic acid molecules separated using formamide. However, the examiner maintains the rejection on the grounds that the motivation existed to combine the references as can be seen in the last paragraph of the rejection and because the claims are not limited to special conditions including both the absence of formamide and the inclusion of other reagents. As such the art as cited, obviates the above claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Sally Sakelaris whose telephone number is (703) 306-0284. The examiner can normally be reached on Monday-Thursday from 7:30AM-5:00PM and Friday from 1:00PM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)308-1119. The fax number for the Technology Center is (703)305-3014 or (703)305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to Chantae Dessau whose telephone number is (703)605-1237.

Sally Sakelaris

12/18/2003

CARLA J. MYERS
PRIMARY EXAMINER